consists of (a) synthesizing a population of target specific nucleic acid probes each having a different specifier; (b) synthesizing a corresponding population of anti-genedigits each having a unique label, the population having a diversity sufficient to uniquely hybridize to genedigits within the specifiers, and (c) hybridizing the populations of target nucleic acid probes to the anti-genedigits, to produce a population in which each of the target specific probes is uniquely labeled. Also provided is a method of detecting a nucleic acid analyte.--

A1 cont.

REMARKS

Claims 1-84 are currently pending in the application, and claims 1-15 and 78-84 are currently under examination.

The specification has been amended to reduce the number of words in the abstract. This amendment merely corrects a formality and does not add new matter. Accordingly, the Applicant respectfully requests that the Examiner enter the amendment. A marked up version of the amended abstract is provided in Appendix A attached hereto.

The Applicant has reviewed the Office Action and respectfully traverses all grounds of objection and rejection to the application for the reasons that follow.

Objection to the Abstract of the Specification

The Office Action states that the abstract of the specification is lengthy exceeding 150 words and correction to reduce the number of words in the abstract is required. The Applicant has amended the abstract herein to contain less than 150 words. Therefore, the Applicant requests that this objection to the specification be removed.

Rejection Under 35 U.S.C. § 112, Second Paragraph

Claims 1-15 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite for reciting the phrases "about thirty or more unique labels," "about 40, 60, 80, 100, 120, and 140" and "about the same unit signal." Specifically, the Office Action alleges that the claims are unclear and indefinite because the term "about" is a relative term with respect to the claimed number of unique labels and it could include any number around the claimed number.

Applicant asserts that the term "about" is sufficiently clear and definite to those skilled in the art. The MPEP 2173.05(b) acknowledges that relative terms such as "about" is clear and definite if one skilled in the art would understand what is claimed in light of the specification. For example, in *Ex parte Eastwood*, 163 USPQ 316 (Bd. App. 168), the term "about" was used to define the area of the lower end of a mold as between 25 to about 45% of the mold entrance and was held to be clear, but flexible. Similarly, in *W.L. Gore & Associates, Inc.*

v. Garlock, Inc. 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), the court held that a limitation defining the stretch rate of a plastic as "exceeding about 10% per second" is definite because infringement could clearly be assessed through the use of a stopwatch.

Applicant submits that the meaning of the term "about" is clear. Specifically, the term "about" means nearly, reasonably close to, or approximately. In particular, Applicant submits that the term "about" in reference to the number of labels would be clear to one skilled in the art based on the teaching in the specification because the specification teaches several specific values for the number of labels. For example, claims 4 and 5, which depend from claim 1, recite that the diverse population of labels of claim 1 can have a diversity selected from a group consisting of about 40, 60, 80, 100, 120, 140, and 150. Therefore, one skilled in the art would understand that "about 30" can include more or less than 30, but would not be boundless because other numbers are specifically recited. In addition, the term "about" in reference to the number of labels and the unit signal is definite because infringement can clearly be assessed by counting the number of labels or the unit signal.

Accordingly, the Applicant submits that the claims are clear and definite and respectfully requests that the rejection of claims 1-15 under 35 U.S.C. § 112, second paragraph, be withdrawn.

Rejections Under 35 U.S.C. § 102(b)

Claims 1-6 stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Chandler WO 99/52708. The Office Action states that Chandler describes microparticles with multiple fluorescent signals. In particular, the Office Action states that Chandler describes a unique population of labels having one or more unique labels bound to DNA (microparticles); unique labels or dyes having unique emission spectra which is unique to the specific set or population; unique labels having a mixture of two or more distinctly labeled particles created through variation of the amount of or type of dye; and labels having fluorescent dyes.

Claims 1-6 of the subject application recite a diverse population of labels having about thirty or more unique labels where each of the unique labels is bound to a nucleic acid molecule. The term "bound" when referring to a unique label or nucleic acid is taught in the specification, for example, at page 6, lines 14-17, as meaning that a label monomer is attached to a nucleotide in a 1:1 correspondence. A label monomer is taught in the specification, for example, at page 6, lines 17-21, as an individual measurable moiety, such as a radioisotope, fluorochrome, dye, enzyme, nanoparticle, chemiluminescent marker, biotin, or other moiety known in the art that is measurable by analytical methods.

Chandler describes the use of dyed core microparticles and the use of carrier microparticles to which nanoparticles

having a plurality of dyes are attached (see page 6, lines 5-8). However, Chandler does not teach a label monomer, such as a flourescent dye molecule, attached to a nucleotide in a 1:1 correspondence as taught and claimed in the subject application. Instead Chandler teaches methods for labeling liquids with fluorescent microparticles where the microparticles are stained with fluorescent dyes in bulk (see page 13, lines 24-37). Because the particles are dyed in bulk, an undetermined plurality of label monomers, such as flourescent dye molecules, are soaked into the particles. Different particles within the population will incorporate different amounts of dyes and thus have a variable amount of label monomers. Chandler does not go on to teach binding a label monomer within a microparticle to a nucleic acid in a 1:1 correlation.

Since the published application by Chandler does not teach each element of the claimed invention, Chandler cannot anticipate the claimed invention. Accordingly, Applicant respectfully requests that this ground of rejection be withdrawn.

Claims 1, 3-7, and 9-12 stand rejected under 35 U.S.C. § 102(e) as allegedly anticipated by U.S. Patent No. 6,428,667 to Glazer et al. The Office Action alleges that Glazer et al. describes multichromophore fluorescent probes having 20, or 100 or more labels presumably bound to a nucleic acid at column 3, lines 4-20, and column 4, lines 3-11. However, Glazer et al. does not describe such probes and the cited passages in Glazer et al. instead describe ring structures of fluorescent monomeric units and polymers having monomeric units. In addition, the

Office Action alleges that Glazer et al. describe fluorescent labels (at column 3, lines 21-22, and column 4, lines 12-17) and that labels contain a mixture of two different labels (at column 6, lines 60-68). Again, the cited passages do not correlate with the teachings of Glazer et al. in U.S. Patent No. 6,428,667.

Glazer et al. describe detecting molecules using fluorescent non-covalently binding and intercalating molecules which have affinity for nucleic acids. In particular, Glazer et al. describe combining compounds such as ethidium dimer with DNA at certain molar ratios of dye compound and DNA (see column 10, lines 7-26) which would not result in a 1:1 correspondence between a label monomer and nucleic acid as taught in the subject application. Indeed, Glazer et al. does not describe any means of sequence specific labeling of nucleic acids which precludes uniquely labeling nucleic acids with more than one label in predetermined proportions. Because the Glazer et al. patent does not teach each element of the claimed invention, the patent to Glazer et al. cannot anticipate the claimed invention. Accordingly, Applicant respectfully requests that this ground of rejection be withdrawn.

In addition, Applicant would like to point out that the subject application was filed on July 3, 2001, and was published on January 16, 2003. Therefore, the application does fall under the American Inventors Protection Act of 1999.

Rejection Under 35 U.S.C. § 103(a)

Claims 7-15 and 78-84 stand rejected under 35 U.S.C. § 103(a) as allegedly obvious over Chandler (WO 99/52708) in view of Chandler et al. (WO 99/37814). The Office Action alleges that Chandler describes a unique or distinct population of labels. However, the Office Action acknowledges that Chandler does not describe labeled probes attached to uniquely labeled microparticles. The Office Action further alleges that Chandler et al. describes microparticles attached with oligonucleotide probes and that it would have been obvious to a person of ordinary skill in the art to combine the labeled microparticles as taught by Chandler with the labeled probes as taught by Chandler et al.

Claims 7-15 of the subject application recite a diverse population of uniquely labeled probes having about thirty or more target specific nucleic acid probes each attached to a unique label bound to a nucleic acid. Claims 78-84 of the subject application recite a nucleic acid labeling kit having a set of genedigits, a set of anit-genedigits and a unique set of labels bound to a nucleic acid. In both sets of claims the unique labels are bound to a nucleic acid. As described previously the term "bound" is taught in the specification as meaning that a label monomer is attached to a nucleotide in a 1:1 correspondence. Neither Chandler nor Chandler et al. teach or suggest a unique label bound to a nucleic acid where a label monomer is attached to a nucleotide in a 1:1 correspondence as taught in the subject application.

The Office Action cites an example in Chandler et al. at page 28, line 19, to page 29, line 26, as evidence that Chandler et al. describes a population of uniquely labeled probes. However, the example described by Chandler et al. does not teach or suggest a 1:1 correspondence between a label monomer and a nucleotide. Instead Chandler et al. describes that a saturating amount of an oligonucleotide is bound to a dyed bead (page 28, lines 26-27). Because Chandler combined with Chandler et al. do not teach or suggest every element of the invention they can not render the invention obvious. In addition, there is no suggestion or motivation to combine Chandler with Chandler et al. Accordingly, the Applicant respectfully requests that this ground of rejection be withdrawn.

CONCLUSION

In light of the Amendments and Remarks herein, the Applicant submits that the claims are now in condition for allowance and respectfully requests a notice to this effect. The Examiner is invited to contact the undersigned agent or Cathryn Campbell with any questions related to this application.

Respectfully submitted,

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Appendix A

A marked up version of the specification follows. Text to be deleted is in brackets.

Please replace the paragraph at page 70, lines 2-29, with the following paragraph:

The invention provides a diverse population of uniquely labeled probes, containing about thirty or more target specific nucleic acid probes each attached to a unique label bound to a nucleic acid. Also provided is a method of producing a population of uniquely labeled nucleic acid probes. The method consists of (a) synthesizing a population of target specific nucleic acid probes each having a different specifier; (b) synthesizing a corresponding population of anti-genedigits each having a unique label, the population having a diversity sufficient to uniquely hybridize to genedigits within the specifiers, and (c) hybridizing the populations of target nucleic acid probes to the anti-genedigits, to produce a population in which each of the target specific probes is uniquely labeled. Also provided is a method of detecting a nucleic acid analyte. [The method consists of (a) contacting a mixture of nucleic acid analytes under conditions sufficient for hybridization with a plurality of target specific nucleic acid probes each having a different specifier; (b) contacting the mixture under conditions sufficient for hybridization with a corresponding plurality of anti-genedigits each having a unique label, the plurality of

anti-genedigits having a diversity sufficient to uniquely hybridize to genedigits within the specifiers, and (c) uniquely detecting a hybridized complex between one or more analytes in the mixture, a target specific probe, and an anti-genedigit.]